WHAT IS CLAIMED IS:

1. A method of treating or preventing stress response in a subject in need thereof, which comprises administering a therapeutically effective amount of a CCR5 antagonist to the subject.

2. The method according to claim 1, wherein the CCR5 antagonist comprises a small molecule organic compound, a polypeptide, or an antibody.

3. The method according to claim 1, wherein the subject is a primate.

4. The method according to claim 1, wherein the subject is other than a graft transplant patient.

5. The method according to claim 1, wherein the stress response is stress response to surgery.

6. The method according to claim 1, wherein the subject is a cardiac surgery patient.

7. The method according to claim 1, wherein the therapeutically effective amount of CCR5 antagonist administered to the subject is an amount effective to inhibit endogenous production of one or more pro-inflammatory cytokines selected from the group consisting of IL1 and IL6.

8. The method according to claim 7, wherein the stress response is stress response to surgery.

9. The method according to claim 7, wherein the subject is other than a graft transplant patient.

10. The method according to claim 1, wherein the CCR5 antagonist is co-administered with a therapeutically effective amount of an immunosuppressive agent.

11. A method of treating or preventing hyperthermia in a subject in need thereof, which comprises administering a therapeutically effective amount of a CCR5 antagonist to the subject.

12. The method according to claim 11, wherein the CCR5 antagonist comprises a small molecule organic compound, a polypeptide, or an antibody.

13. The method according to claim 11, wherein the subject is a primate.

14. The method according to claim 11, wherein the subject is other than a graft transplant patient.

15. The method according to claim 11, wherein the stress response is surgical hyperthermia.

16. The method according to claim 11, wherein the subject is a cardiac surgery patient.

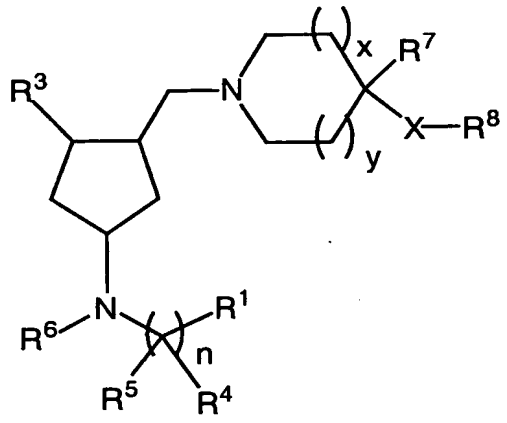
17. The method according to claim 11, wherein the therapeutically effective amount of CCR5 antagonist administered to the subject is an amount effective to inhibit endogenous production of one or more pro-inflammatory cytokines selected from the group consisting of IL1 and IL6.

18. The method according to claim 17, wherein hyperthermia is surgical hyperthermia.

19. The method according to claim 18, wherein the subject is other than a graft transplant patient.

20. The method according to claim 11, wherein the CCR5 antagonist is co-administered with a therapeutically effective amount of an immunosuppressive agent.

21. A method of treating or preventing stress response which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt or an individual diastereomer thereof:



(I)

wherein:

X is selected from: -(C_{0-6} alkyl)-Y-(C_{0-6} alkyl)-,
-(C_{0-6} alkyl)-C_{3-8} cycloalkyl-(C_{0-6} alkyl)-,
C_{2-10} alkenyl, and C_{2-10} alkynyl,
where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:
(a) halo,
(b) hydroxy,
(c) -O-C_{1-3} alkyl, and
(d) trifluoromethyl,

and where Y is selected from:
a single bond, -O-, -SO_2-, -NR^{10}-, -NR^{10}-SO_2-, -SO_2-NR^{10}-,
-S-, and -SO-,

and where R^{10} is independently selected from: hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{5-6} cycloalkyl, benzyl, phenyl, and C_{1-6} alkyl-C_{3-6} cycloalkyl,

which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, C_{1-3} alkyl, C_{1-3} alkoxy and trifluoromethyl;

R^1 is selected from:

(1) $-CO_2H$,

(2) $-NO_2$,

(3) -tetrazolyl,

(4) -hydroxyisoxazole,

(5) $-SO_2NHCO-(C_{0-3}$ alkyl)$-R^9$, wherein R^9 is independently selected from: hydrogen, C_{1-6} alkyl, C_{5-6} cycloalkyl, benzyl or phenyl, which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, C_{1-3} alkyl, C_{1-3} alkoxy and trifluoromethyl, and

(6) $-P(O)(OH)_2$;

R^3 is selected from the group consisting of:

phenyl and heterocycle,

which is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

(a) halo,

(b) trifluoromethyl,

(c) hydroxy,

(d) C_{1-3} alkyl,

(e) $-O-C_{1-3}$ alkyl,

(f) $-CO_2R^9$,

(g) $-NR^9R^{10}$, and

(h) $-CONR^9R^{10}$;

R^4, R^5 and R^6 are independently selected from:

hydrogen, C_{1-10} alkyl, C_{3-8} cycloalkyl, C_{2-10} alkenyl,

C_{2-10} alkynyl, phenyl, -(C_{1-6} alkyl)-phenyl,
-(C_{1-6} alkyl)-C_{3-8} cycloalkyl, naphthyl, biphenyl, and heterocycle,
which is unsubstituted or substituted with 1-7 of R^{11} where R^{11} is independently selected from:

(a) halo,
(b) trifluoromethyl,
(c) hydroxy,
(d) C_{1-3} alkyl,
(e) -O-C_{1-3} alkyl,
(f) -CO_2R^9,
(g) -NR^9R^{10}, and
(h) -$CONR^9R^{10}$,

or where R^4 and R^5 may be joined together to form a 3-8 membered saturated ring which may be unsubstituted or substituted with 1-7 of R^{11},
or where R^5 and R^6 may be joined together to form a 3-8 membered saturated ring which may be unsubstituted or substituted with 1-7 of R^{11};

R^7 is selected from:

(1) hydrogen,
(2) C_{1-6} alkyl, which is unsubstituted or substituted with 1-4 substituents where the substituents are independently selected from: hydroxy, cyano, and halo,
(3) hydroxy, and
(4) halo;

R^8 is selected from:
hydrogen, C_{3-8} cycloalkyl, phenyl, naphthyl, biphenyl, and heterocycle,
which is unsubstituted or substituted with 1-7 of R^{12} where R^{12} is independently selected from:

(a) halo,
(b) cyano,
(c) hydroxy,
(d) C_{1-6} alkyl, which is unsubstituted or substituted with 1-5 of R^{13} where R^{13} is independently selected from: halo, cyano,

hydroxy, C_{1-6} alkoxy, $-CO_2H$, $-CO_2(C_{1-6}$ alkyl), trifluoromethyl, and $-NR^9R^{10}$,

(e) $-O-C_{1-6}$ alkyl, which is unsubstituted or substituted with 1-5 of R^{13},

(f) $-CF_3$,

(g) $-CHF_2$,

(h) $-CH_2F$,

(i) $-NO_2$,

(j) C_{0-6} alkyl-phenyl or C_{0-6} alkyl-heterocycle, which is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

(i) halo,

(ii) hydroxy,

(iii) C_{1-6} alkyl, unsubstituted or substituted with 1-5 substituents, each of which is independently selected from halo, cyano, hydroxy, C_{1-6} alkoxy, $-CO_2H$, $-CO_2(C_{1-6}$ alkyl), trifluoromethyl, and $-NR^9R^{10}$,

(iv) $-O-C_{1-6}$ alkyl,

(v) $-CF_3$,

(vi) $-OCF_3$,

(vii) $-NO_2$,

(viii) $-CN$,

(ix) $-SO_2-C_{1-6}$ alkyl,

(x) $-CO_2R^9$,

(xi) $-NR^9R^{10}$,

(xii) $-CONR^9R^{10}$,

(xiii) $-SO_2-NR^9R^{10}$,

(xiv) $-NR^9-SO_2-R^{10}$,

(xv) $-C_{3-8}$ cycloalkyl,

(xvi) $-OC_{3-8}$ cycloalkyl, and

(xvii) phenyl;

(k) $-CO_2R^9$,

(l) tetrazolyl,

(m) $-NR^9R^{10}$,

(n) $-NR^9-COR^{10}$,
(o) $-NR^9-CO_2R^{10}$,
(p) $-CO-NR^9R^{10}$,
(q) $-OCO-NR^9R^{10}$,
(r) $-NR^9CO-NR^9R^{10}$,
(s) $-S(O)_m-R^9$, wherein m is an integer selected from 0, 1 and 2,
(t) $-S(O)_2-NR^9R^{10}$,
(u) $-NR^9S(O)_2-R^{10}$,
(v) $-NR^9S(O)_2-NR^9R^{10}$,
(w) C_{1-6} alkyl substituted with $-C_{3-8}$ cycloalkyl, and
(x) $-C_{3-8}$ cycloalkyl;

n is an integer selected from 1, 2, 3 and 4;
x is an integer selected from 0, 1 and 2, and y is an integer selected from 0, 1 and 2, with the proviso that the sum of x and y is 2.

22. The method according to claim 21, wherein the subject in need of treatment is other than a graft transplant patient.

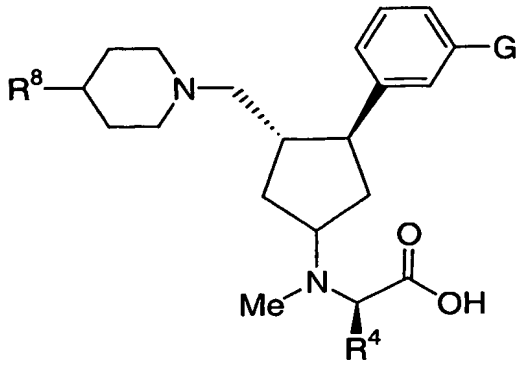
23. The method according to claim 21, wherein the stress response is stress response to surgery.

24. The method according to claim 21, wherein the subject in need of treatment is a cardiac surgery patient.

25. The method according to claim 21, wherein the stress response comprises hyperthermia.

26. The method according to claim 21, wherein the therapeutically effective amount of the compound of Formula (I) administered to the subject is an amount effective to inhibit endogenous production of one or more pro-inflammatory cytokines selected from the group consisting of IL1 and IL6.

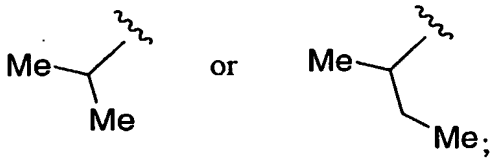
27. A method of treating or preventing stress response which comprises administering to a subject in need of such treatment a therapeutically effective amount of a compound of Formula (II), or a pharmaceutically acceptable salt thereof:



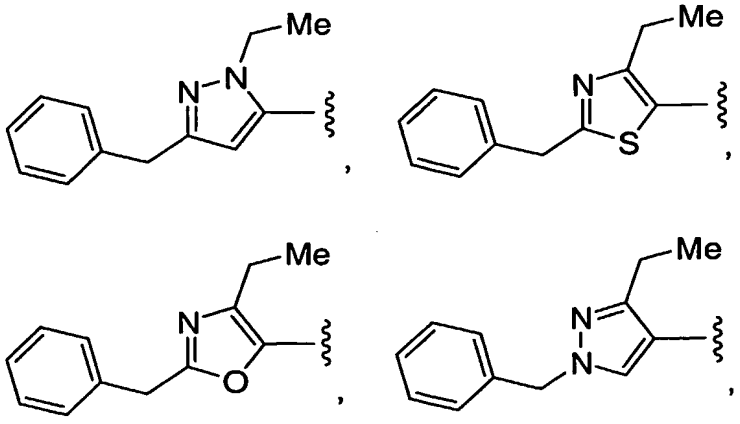
(II);

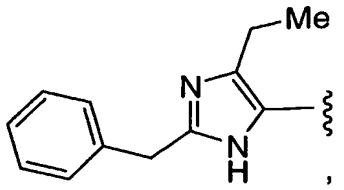
wherein

R^4 is



R^8 is selected from the group consisting of

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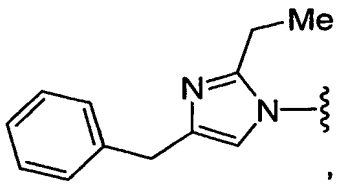
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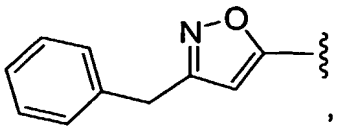
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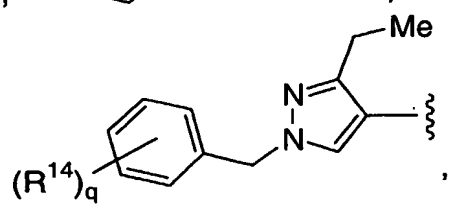
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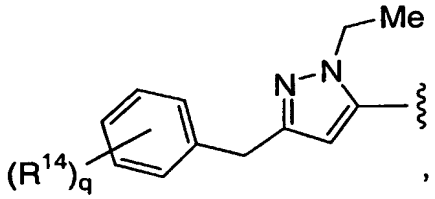
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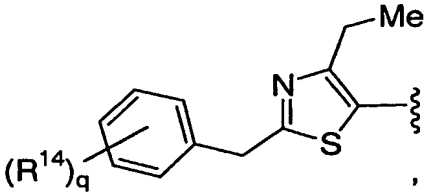
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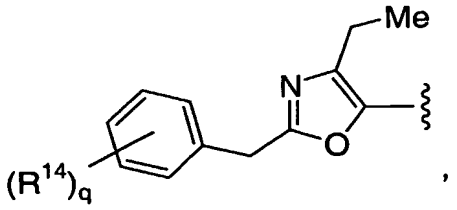
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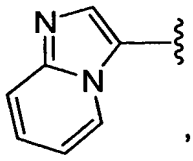
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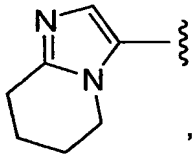
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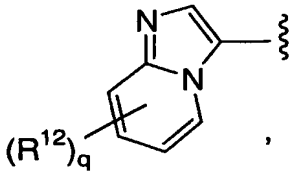
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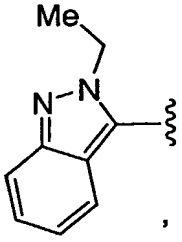
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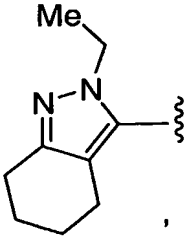
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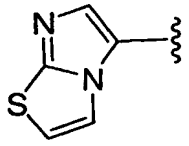

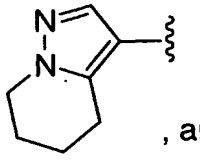
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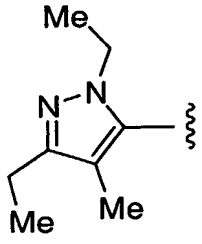


10 ;

R^{12} and R^{14} are each independently selected from the group consisting of F, Cl, CF_3, OCH_3, OCH_2CH_3, OCF_3, O-cyclobutyl, CN, O-cyclopropyl, CH_3, CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$, and SO_2CH_3;

G is hydrogen or fluoro; and

q is an integer equal to 1 or 2.

28. The method according to claim 27, wherein the subject in need of treatment is other than a graft transplant patient.

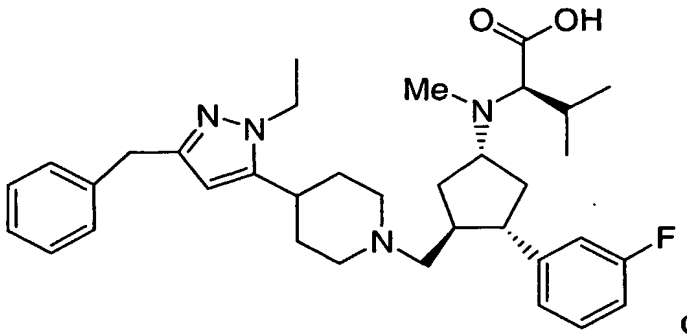
29. The method according to claim 27, wherein the stress response is stress response to surgery.

30. The method according to claim 27, wherein the subject in need of treatment is a cardiac surgery patient.

31. The method according to claim 27, wherein the stress response comprises hyperthermia.

32. The method according to claim 27, wherein the therapeutically effective amount of the compound of Formula (II) administered to the subject is an amount effective to inhibit endogenous production of one or more pro-inflammatory cytokines selected from the group consisting of IL1 and IL6.

33. A method of treating or preventing stress response which comprises administering to a subject in need of such treatment a therapeutically effective amount of Compound A:



Compound A;

or a pharmaceutically acceptable salt thereof.

34. The method according to claim 33, wherein the subject in need of treatment is other than a graft transplant patient.

35. The method according to claim 33, wherein the stress response is stress response to surgery.

36. The method according to claim 33, wherein the subject in need of treatment is a cardiac surgery patient.

37. The method according to claim 33, wherein the stress response comprises hyperthermia.

38. The method according to claim 33, wherein the therapeutically effective amount of Compound A administered to the subject is an amount effective to inhibit endogenous production of one or more pro-inflammatory cytokines selected from the group consisting of IL1 and IL6.

39. A method of treating or preventing a disorder characterized by the activity of at least one pro-inflammatory cytokine selected from the group consisting of IL1 and IL6, in a mammal in need of such treatment or prevention, which comprises administering to the subject a CCR5 modulator in an amount effective to inhibit endogenous production of the cytokine.

40. The method according to claim 39, wherein the CCR5 modulator comprises a CCR5 antagonist.

41. The method according to claim 39, wherein the disorder being treated or prevented is selected from the group consisting of post-surgical inflammatory response, sepsis, septic shock, and ARDS.

42. A method of inhibiting endogenous production of at least one pro-inflammatory cytokine selected from the group consisting of IL1 and IL6, which comprises administering to a mammal in need of such inhibition a CCR5 modulator in an amount effective to inhibit production of the cytokine.

43. The method according to claim 42, wherein the CCR5 modulator comprises a CCR5 antagonist.

44. A method for monitoring the effectiveness of treatment of a subject suffering from an acute inflammatory response, said treatment comprising administration of a CCR5 modulator, wherein the method comprises:

(A) obtaining a pre-administration sample from the subject prior to administration of the CCR5 modulator and determining the level of expression or activity of a pro-inflammatory cytokine selected from the group consisting of IL1 and IL6 in the pre-administration sample;

(B) obtaining a post-administration sample from the subject subsequent to administration of the CCR5 modulator and determining the level of expression or activity of the pro-inflammatory cytokine; and

(C) comparing the level of cytokine expression or activity of the post-administration sample with the level of cytokine expression or activity of the pre-administration sample.

45. The method according to claim 44, which further comprises:

(D) adjusting the administration of the CCR5 modulator to increase or decrease the level of cytokine expression or activity; and

(E) repeating steps (A), (B), and (C).

46. The method according to claim 45, wherein the CCR5 modulator comprises a CCR5 antagonist.

47. A method for determining the efficacy of a CCR5 modulator in correcting an abnormal level of a pro-inflammatory cytokine selected from the group consisting of IL1 and IL6 in a subject in need of such correction, which comprises:

(A) administering an amount of the CCR5 modulator to the subject; and

(B) determining the level of the cytokine in the subject following administration of the CCR5 modulator, wherein a change in the cytokine level toward a normal level is a measure of the efficacy of the modulator.

48. The method according to claim 47, which is a method for determining the efficacy of a CCR5 antagonist in reducing an abnormally high level of a pro-inflammatory cytokine selected from the group consisting of IL1 and IL6 in a subject in need of such reduction, which comprises:

(A) administering an amount of the CCR5 antagonist to the subject; and

(B) determining the level of the cytokine in the subject following administration of the CCR5 antagonist, wherein a reduction in the cytokine level toward a normal level is a measure of the efficacy of the antagonist.

49. A method of treating a post-trauma inflammatory response in a subject undergoing or having undergone a multiple trauma associated with a high risk of sepsis or ARDS, which comprises administering to the subject a therapeutically effective amount of a CCR5 antagonist.

50. The method according to claim 49, wherein the trauma comprises pelvic or multiple long bone fracture, massive blood loss, multiple unit blood transfusion, prolonged hypotension/shock, or pulmonary contusion.

51. A method for treating or preventing stress response in a subject in need thereof, which comprises administering to the subject a CCR5 antagonist in an amount effective to inhibit endogenous production of prostaglandin E2.

52. The method according to claim 51, wherein the stress response comprises a febrile response.